A Clinicopathological Study of Abnormal Uterine Bleeding in Peri and Post Menopausal Age Group, with Special Emphasis on Early Diagnosis of Uterine Malignancy

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ABSTRACT

Introduction: Abnormal uterine bleeding (AUB) continues to be one of the most frequently encountered problems in gynaecology. The present clinicopathological study was planned for early diagnosis and proper treatment of the organic pathology of the genital tract, with special emphasis on early diagnosis of malignancy.

Material and Methods: The patients included in this study belong to Peri and Post menopausal age group starting from 40 years or, more and presenting with abnormal uterine bleeding. These patients were subjected to a detailed history and a meticulous general, systemic and local examination along with the relevant investigations including endometrial aspiration smear / microbiopsy, dilatation and curettage, and biopsy.

Results: Total 300 patients were included in this study. Dysfunctional Uterine Bleeding and Menorrhagia were the most common diagnosis (39%) and complaint respectively. Out of 300 cases, 169 (56.3%) cases were managed surgically by total abdominal hysterectomy (138), vaginal hysterectomy (19) and extended hysterectomy (12). In the rest of 131 patients, 128 (42.6%) cases underwent diagnostic as well as therapeutic D and C and 3 cases were managed conservatively with radiotherapy. Fibroid uterus, chronic cervicitis and proliferative endometrium were the most common myometrial, cervical and endometrial histopathology respectively.

Conclusion: All cases of AUB in the peri and post menopausal age group should be thoroughly analyzed including complete history, detailed clinical examination followed by appropriate radiological and pathological examination, especially in suspicious cases for early detection of premalignant and malignant lesions of the body of uterus, leading to early diagnosis and prompt treatment at appropriate time.

Keywords: Abnormal Uterine Bleeding, Post Menopause, Endometrial Hyperplasia, Cervicitis, Fibroid Uterus, Adenomyosis.

INTRODUCTION

Abnormal uterine bleeding (AUB) continues to be one of the most frequently encountered and perplexing problems in gynaecology and most of the patients attend the gynaecology clinics with only this complaint. Abnormal uterine bleeding as such is a symptom and not a disease and various types of presentations according to the severity and cycles are – menorrhagia, polymenorrhoea, polymenorrhagia, metrorrhagia, contact bleeding, continuous bleeding per vaginum, blood stained discharge and post menopausal bleeding.

Its various causative factors are Benign lesions (Fibroid, Endometriosis, Cervical polyps, Endometrial polyps, etc.), Dysfunctional Uterine Bleeding (DUB) Malignant lesions

(Carcinoma body of uterus, Leiomyosarcoma, Carcinoma Cervix), Inflammatory, Traumatic, Ovarian tumors, and Miscellaneous causes (Estrogen therapy, Bleeding disorders, Pregnancy complications, etc.). This can occur at any age and the causes can be reshuffled according to the age group. The present clinicopathological study of abnormal uterine bleeding above 40 year of age was planned for early diagnosis and proper treatment of the organic pathology of the genital tract, with special emphasis on early diagnosis of malignancy.

MATERIAL AND METHODS

A total of three hundred (300) patients attending the OPD of obstetrics and gynaecology were included in this study. They were stratified according to their age and presenting complaint; those patients belonging to Peri and Post menopausal age group starting from 40 years or, more and presenting with abnormal uterine bleeding were selected for the study. A well defined study protocol was designed at the start of the study. All the patients were evaluated according to the protocol which started with personnel data collection through personnel interview with each patient. These patients were subjected to a detailed history and a meticulous general, systemic and local examinations along with the relevant investigations including endometrial aspiration smear / microbiopsy, dilatation and curettage, biopsy, ultrasound (USG) and computerized tomography (CT scan). Then the patients were followed up for the appropriate managements. Further the histopathological results were analyzed according to the management done. In the last detailed correlation was done among all the available data related to clinical, radiological, pathological and final assessments.

STATISTICAL ANALYSIS

Simple statistical calculations (as mentioned below) were done in this study.

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A) Percentage Value of a Specified Category

Number of cases of the specified category / Total number of cases x 100.

B) Percentage Accuracy of a Test

Number of cases of a specific pathology diagnosed with the test (Ex. USG) / Total number of True cases of that specified pathology x 100.

C) Percentage Correlation of Investigation 1 with Investigation 2

Number of cases of a specified pathology diagnosed with Investigation 1 (Ex. Cytology) / Number of cases of that specified pathology diagnosed with Investigation 2 (Ex. Histology) x 100.

RESULT

Among 300 patients, USG was performed in 150 cases and in 120 cases endometrial aspiration cytology and micro biopsy was done. A clinical, radiological and pathological correlation was done in all cases. DUB was the most common diagnosis (39%), followed by Fibroid uterus, seen in 28% cases. Malignancy was diagnosed in 18 (6%) cases in our study, out of which 4 cases had carcinoma body of uterus. Maximum Number of cases (69.2%) belonged to the age group of 41-45 years and the least number was seen in the more than 60 years category (5.4%). Para 3 and para 4 together constituted the largest group (51.7%), while only 2% cases were nulliparous. Menorrhagia was the most common complaint, seen in 30.7% of cases, followed by polymenorrhoea (21.6%) and polymenorrhagia (16.6%). There were 22 (7.3%) cases of post menopausal bleeding in our study. In the perimenopausal age group (41-50 years), 59.8% patients presented with menorrhagia and / or, polymenorrhoea, while in the post menopausal age group (>50 years) maximum number of patients (68.6%) presented with blood stained discharge and / or, post menopausal bleeding. In this category, there was no case of continuous bleeding P/V. Excessive discharge P/V associated with AUB was the most common additional complaint, seen in 29% cases. Per speculum examination revealed cervical erosion in 36% cases and polyp in 4.3% cases. On per vaginum examination, uterus was found to be normal in size in 42.3% cases and atrophic in 10% cases. Uterus was freely mobile in 81.3% cases and 15% cases revealed an adenexal mass (follicular cysts, corpus leuteum cysts, simple serous cysts, serous cystadenoma). Parametrial involvement in cases of malignancy was judged by per rectal examination and revealed 3 cases with parametrial extension. Ultrasonic examination is very useful in the diagnosis of uterine size especially in obese patients, and 82.05% accuracy rate in the detection of fibroid uterus was obtained in our study. Cases of adenomyosis had a 39.5% rate of diagnostic accuracy by USG. However, it could diagnose cases of endometrial hyperplasia which were earlier categorized under the head of DUB. At times, it was difficult to differentiate a mass in the uterus with carcinoma body uterus and it revealed only a 50% accuracy rate, while the number of cases was very less (2). CT scan was performed in 3 cases in our study. One case had carcinoma body of uterus and 2 cases had advanced carcinoma cervix. The one case of endometrial carcinoma showed no abnormality on CT scan examination. The other two cases of advanced carcinoma cervix revealed an enlarged cervix with an enlarged uterus. In both cases bilateral parametrium was involved and few lymph nodes in the illiac group were found to be enlarged. The pelvic walls, bladder and rectum were however, free from the disease process. Thus in such cases, CT scan was helpful in staging of the disease and planning of the treatment.

Endometrial aspiration study was performed in 120 cases and 18.3% cases revealed an unsatisfactory smear with a 91.3% correlation was obtained in cases of hyperplasia. Cases of malignancy showed a 100% correlation. Out of 300 cases, 169 (56.3%) cases were managed surgically by total abdominal hysterectomy (138), vaginal hysterectomy (19) and extended hysterectomy (12). In the rest of 131 patients, 128 (42.6%) cases underwent diagnostic as well as therapeutic D and C and 3 cases were managed conservatively with radiotherapy. Fibroid uterus alone was the most common myometrial pathology seen in 44.4% cases, followed by adenomyosis alone (18.3% cases). Myometrial invasion by carcinoma was seen in 2.4% cases. Chronic cervicitis was the most frequently occurring cervical lesion on histopathology seen in 51.2% cases. These cases presented either as cervical erosion (88.5%) or cervical ulcer (11.5%) clinically. Out of 14 cases of carcinoma cervix, 12 (85.7%) cases presented with a cervical growth and 2 (14.3%) cases presented with a cervical ulcer. Endometrial histopathology was studied in 297 cases and proliferative endometrium was the most common pattern seen in 49.8% cases. Hyperplasia was observed in 18.5% cases and malignancy in 1.7% cases. Perimenopausal patients (41-50 years) showed a predominantly normal endometrial pattern (proliferative and secretory) in 69.5% cases. Hyperplasia was observed in 18.8% cases, while 3 cases of endometrial carcinoma were seen in this age group. The post menopausal age group (>50 years), however, showed 19.04% cases of hyperplasia and 1 case of endometrial carcinoma in our study. Out of 117 cases of DUB, proliferative type of endometrium was seen in 46.15% cases of DUB, and 17% cases had hyperplastic type of endometrium. TB endometrium was found to occur in only 1 (0.85%) case. Inflammatory lesions (TB endometrium) and endometrial polyp could not be diagnosed clinically and their diagnosis rested on histopathological examination. Fibroid uterus and adenomyosis were difficult to differentiate clinically and required use of other diagnostic modalities like USG. Carcinoma endometrium could be diagnosed in 2 cases only clinically, out of a total number of 4 cases. On analysis of the patients with endometrial carcinoma, it was seen that 1 out of 4 cases presented with post menopausal bleeding and 2 were less than para 3. "Corpus Cancer Syndrome" was observed in 2 cases. All patients were diagnosed on pathological examination by endometrial aspiration smear study and microbiopsy, and were treated by extended hysterectomy.

DISCUSSION

Abnormal Uterine Bleeding (AUB) is the most common clinical presentation of gynaecological cases, in peri and post menopausal age. Therefore to reach an early diagnosis

at proper time is essential in these cases for appropriate treatment. In the present study on AUB, 300 cases were investigated and a clinicopathological correlation was done.

Distribution of Cases

On analyzing the various disease incidences and comparing them with those of *Patra and Giri*, ² *Sarin et al*, ³ and *Tyagi SP et al*, ⁴ it was seen that like there study, DUB was the most common disease entity (39%) in our study also (Table 1).

Age Incidence

The highest number of cases in this study belonged to the age group 41-45 years (69.2%). This fact has been seen by other authors like *Patra and Giri et al*,² *Yusuf et al*,⁵ *and Muzaffar et al*,⁶ in whose studies the largest number of cases belonged to 40-50 years category (Table 1).

Parity

Para 3 group had the highest number of cases (27%), while nulliparous women constituted only 2% cases in our study. Similar findings have been reported by *Sagar S*.⁷

Menstrual Abnormalities

Menorrhagia was the most common complaint occurring in 30.7% cases in our study. Menorrhagia has been noted as the most common complaint in other studies too, like that of *Sagar S*,⁷ in which it accounted for 40.6% of the complaint and *Tyagi SP et al*,⁴ in which it appeared in 41.3% cases (Table 1).

Relation of Bleeding Patterns with Age

Menorrhagia and polymenorrhoea was the most prominent type (59.8%) of AUB in the peri menopausal age group. Post Menopausal Bleeding (41.2%) was most common form of bleeding after the age of 50 years. No case of continuous bleeding P/V was observed after the age of 50 years. This has also been reported by *Sagar S.*⁷ *Sagar S*⁷ also observed that over 90% cases of ten patients with menorrhagia were less than 50 years old.

Internal Examination

Per Speculum Examination

In our study, cervical erosion was seen in 36% cases. *Sagar* S^7 found it in 20.8% cases in her study. Cervical polyp was observed in 4.3% of our patients. A similar incidence of about 6% has been given by *Sagar S* in her study.⁷

Healthy vaginal mucosa was observed in most of our cases (64.3%). Abnormal discharge was noted in 21.7% of our study, due to local infections.

Per Abdominal and Per Vaginum Examination Uterine Size

In our study, uterus was found to be absent in 1 (0.3%) case, in which hysterectomy had been performed and the vault bleeding was due to squamous cell carcinoma. Uterus was found to be atrophic and small in 10% cases belonging to the post menopausal age group. It was normal in size showing no gynaecological pathology i.e. cases of DUB in 42.3% cases.

Lesions	Sarin et al ³	Patra and Giri ²	Tyagi SP et al ⁴	Present Study	
Total Cases	750	195	195 104		
Prolapse with Ulcer	6.7%	-	-	6.3%	
Fibroid Uterus	-	27.6%	31.8%	28%	
Endometriosis	-	7.18%	-	10.3%	
Cervical Polyp	-	9.6%	-	05%	
Endometrial Polyp	-	6.1%	2.9%	03%	
TB Endometrium	-	1.02%	1.9%	0.33%	
DUB	-	57.9%	54.8%	39%	
Uterine Malignancy	8.8%	-	4.9%	1.3%	
Carcinoma Cervix	31.2%	-	0.9%	4.6%	
Age Groups	Sarin et al ³	Patra and Giri ²	Tyagi SP et al ⁴	Present Study	
<40	-	28.7%	46.2%	-	
41-45	-	38.2%	25.9%	69.2%	
46-50	-			13.6%	
51-55	6.06%	11.8%	8.9%	5.4%	
56-60	2.33%			6.4%	
>60	2.06%		0.9%	5.4%	
Lesions	Sarin et al ³	Solapurkar ML ²³	Tyagi SP et al ⁴	Present Study	
No. Of Cases	488	1084	104	300	
Menorrhagia	40.9%	25.9%	41.3%	30.7%	
Polymenorrhoea	9.7%	10.1%	13.5%	21.6%	
Polymenorrhagia	16.8%	-	12.5%	16.6%	
Metrorrhagia	19.7%	5.5%	15.4%	6.6%	
Continuous Bleeding P/V	5.1%	-	7.7%	7.6%	
Contact Bleeding	1.02%	-	-	03%	
Blood Stained Discharge	0.4%	-	-	6.3%	
Post Menopausal Bleeding (PMB)	10.4%	08%	9.6%	7.3%	
Bleeding From Vault	-	-	-	0.3%	
Miscellaneous	-	51.4%	-	-	

A normal sized uterus was observed in 40.5% cases by *Patra and Giri*² and in 40.7% cases by *Sagar S*² in their study. According to *Jeffcoates*, AUB associated with a bulky uterus and watery discharge, is strongly suggestive of malignancy.

Adenexal Mass

Adenexal mass was palpable in 15% cases in our series. *Patra and Giri*² observed adenexal pathology in 17.9% cases, while *Sarin*³ found it in only 4.5% of her cases.

Ultrasonography

The diagnostic accuracy of USG in the detection of fibroid uterus was 82.05% in our study. The diagnostic accuracy of identifying leiomyoma by USG has been shown to be 90% by *Lawson TL and Albarelli JN*.9 The differentiation of adenomyosis from myomas is difficult on USG, as seen in our study, in which there was a 39.5% rate of mistaken diagnosis in cases of adenomyosis. A similar rate has been reported by *Fleischer AC et al*.^{10,11}

Computerized Tomography (CT) Scan

CT scan was performed in 3 cases in our study. One case had carcinoma body of uterus and 2 cases had advanced carcinoma cervix. The one case of endometrial carcinoma showed no abnormality on CT scan examination. The Parametrium, bladder and pelvic walls were free from the disease. The other two cases of advanced carcinoma cervix revealed an enlarged cervix with an enlarged uterus, both of which appeared inhomogeneous with a few low density areas (suggestive of malignancy). In both cases bilateral parametrium was involved and few lymph nodes in the illiac group were found to be enlarged. The pelvic walls, bladder and rectum were however, free from the disease process.

Endometrial Aspiration Cytology

In the present study, the failure rate to obtain an adequate smear was 18.3%. Other authors have also reported similar percentage of not getting adequate endocervical smears {10.82% *Torres et al*¹²; 24% *Rao et al*¹³; 10% *Sharma and Laghate*¹⁴}.

The diagnostic accuracy rate was 100% in cases of malignancy, which was similar to the observation of the other authors {Ambiya and Shroff¹⁵; Agarwal et al¹⁶; Chakravarty et al¹⁷; Sharma and Laghate¹⁴}. Bhandari et al¹⁸ have reported the accuracy rate of endometrial aspiration cytology in the diagnosis of endometrial carcinoma as 93.75%.

Management of Patients

Out of the 300 patients, 3 patients were managed conservatively. These included 1 patient who presented with bleeding from the vault and 2 cases of advanced carcinoma cervix, which were all referred for radiotherapy.

Dilatation and curettage was performed in 128 (42.6%) cases, which was both diagnostic and therapeutic. One hundred sixty nine (56.3%) cases underwent operative procedures. Out of these, 138 cases underwent total abdominal hysterectomy, 19 cases had vaginal hysterectomy and 12 cases had an extended hysterectomy.

In the study conducted by *Sagar S*,⁷ 63.94% patients underwent non surgical procedures while the rest i.e. 43.66% underwent hysterectomy.

Myometrial Patterns In Operated Cases

Out of the 300 cases, 169 cases were operated in which the myometrial pattern could be made out. In these cases, fibroid uterus was the most common pathology, seen in 44.37% cases, followed by adenomyosis in 18.3% cases. These findings are closely mimicked by the findings of $Sagar S^7$ as shown in Table 2.

Cervical Lesions On Histopathology

Out of 170 cases, in which the cervix was examined histopathologically, the largest number of cases had chronic cervicitis (51.2%). Cervical polyp was found in 8.9% cases and 6.8% cases had cervical carcinoma. Squamous metaplasia was the least common pathology, which was seen in only 2.38% of the cases.

Sagar S⁷ has observed similar histopathological findings, with the maximum number of cases showing chronic cervicitis (94.04%) in her study.

Histopathological Study of Endometrium

Proliferative endometrium is the most common type (49.83%) in our study. This fact has also been seen by other workers [*Pinto Rosario* (35%), *Nayak et al* (48.7%), *Sagar S* (48.5%), *Patra and Giri* (38.4%), *Solapurkar* (21.4%), and *Tyagi S.P.* (30.8%)] [Table 3]. In the present series, endometrial carcinoma was found in 1.3% cases. The incidence of endometrial carcinoma in cases of AUB varies widely in different studies. While authors like *Solapurkar*²³ reported endometrial carcinoma in 0.6% cases, *Sarin et al*³ and *Lidor*²¹ in their study concentrated on post menopausal bleeding group and reported it as 8.4% and 7% respectively.

Histopathological Status of Endometrium In Cases of DUB

There were 117 cases of DUB seen in our study and 66.6% cases had a normal endometrium (proliferative and secreto-

Sagar S ⁷	Present			
	Study			
45(24.45)	50(29.5)			
66(35.85)	75(44.37)			
40(21.73)	31(18.34)			
02(1.08)	04(2.36)			
00(0)	09(5.32)			
Sutherland	Present			
Series II ²⁴	Study			
All Age	Above 40			
Groups	Years			
54.7%	66.6%			
26.5%	17.09%			
2.6%	11.11%			
-	1.7%			
1.0%	1.7%			
11%	0.85%			
1.1%	-			
1.0%	0.85%			
0.8%	-			
Complications of pregnancy				
entages.				
	66(35.85) 40(21.73) 02(1.08) 00(0) Sutherland Series II ²⁴ All Age Groups 54.7% 26.5% 2.6% - 1.0% 11% 1.1% 1.0% 0.8%			

Table-2: Myometrial and Endometrial Patterns In Operated Cases

	Suther- land Series	Mu- zaffar et al ⁶	Nayak et al ²⁰	Sagar S ⁷	Sarin et al ³	Patra and Giri ²	Lidor ²¹	Do- raiswami et al ²²	Tyagi S.P. ⁴	Pres- ent Study
	III^{19}									
No. Of Cases	1000	260	224	488	750	195	221	409	104	300
Proliferative	64.8	25.8	48.7	48.5	41.1	38.4	-	20.5	30.8	49.83
Secretory	-	35.4	48.7	48.5	41.1	38.4	-	06	30.8	15.15
Hyperplastic	19.5	24.7	10.7	18.2	20.1	6.6	15	06	20.2	18.51
Endometrial Carcinoma	2.3	-	0.9	1.4	8.4	-	07	4.4	2.9	1.3
Squamous Cell CA	-	0.4	-	0.6	12.5	-	-	-	0.9	0.3
Endometrial Sarcoma	-	-	-	0.2	-	-	-	-	0.9	-
Chorio Carcinoma	-	0.4	0.4	-	-	-	-	-	0.9	-
Irregular Shedding	-	-	-	-	-	-	-	-	7.7	0.67
Irregular Ripening	-	-	-	-	-	-	-	-	-	4.7
TB Endometritis	0.9	-	-	0.6	-	1.02	-	-	3.8	0.33
Endometrial Polyp	1.8	1.2	1.8	-	-	6.2	-	11.2	2.9	3.03
Decidual Reaction	-	-	-	1.8	2.4	-	-	22.7	0.9	-
Endometritis	-	13	-	0.4	-	-	-	4.16	0.9	-
Non Specific Endometritis	04	-	-	-	6.8	7.7	-	-	-	0.67
Atrophic Endometrium	4.9	-	5.8	4.1	4.1	-	45	2.5	0.9	5.05
Stellar Reaction	-	0.8	-	-	-	-	-	-	0.9	-
Leiomyosarcoma	-	-	-	-	-	-	-	-	-	-
Miscellaneous	1.8	3.5	7.2	4.0	4.6	7.7	38	22.5	-	0.67
Table-3: Histopathological Status Of Endometrium In Cases Of AUB										

Endometrium	No. of Cases	Peri Menopausal (41-50)	Post Menopausal (>50)
Proliferative	148	134	14
Secretory	45	39	06
Atrophic	15	04	11
Hyperplasia	55	47	08
Simple	38	35	03
Complex	13	10	03
Atypical	04	02	02
Malignancies			
Carcinoma body of uterus	04	03	01
Infiltrating Squamous Cell CA Cervix	01	0	01
Other Lesions	29		
Irregular Ripening	13	07	-
Irregular Shedding	02	02	-
TB Endometritis	01	01	-
Endometrial Polyp	09	08	01
Pill Effect	02	02	-
Chronic Endometritis	02	02	-
Total	297	249	42

ry), while 17.09% cases had hyperplasia. These findings can be compared with those of the famous *Sutherland Series II* 24 given in Table 2.

Endometrial Histology in relation to Age Groups

On analyzing the endometrial histology in relation to various age groups (Table 4), it was found that the incidence of hyperplastic endometrium in the peri menopausal age group was 18.8%, whereas in the post menopausal age group, it was 19.04%. *Solapurkar*,²³ in her series, reported the incidence of hyperplastic endometrium in age groups below and above 35 years as 14.1% and 41.7% respectively. *Pinto Rosario*²⁵ also has shown a relative preponderance of hyperplastic endometrium in patients above 40 years of age (37.9%) than those below it (23.8%).

Malignancies of the uterus were predominant in the peri menopausal age group with 3 out of 4 cases of carcinoma body of uterus being less than 50 years of age. The result of this study was almost similar to data mentioned by *Yusuf et al*,⁵ and *Escoffery et al*,²⁶ in their study. Lesions such as TB endometritis, irregular ripening and irregular shedding were diseases of the peri menopausal age group. *Solapurkar*²³ observed 10 out of 13 (76.9%) cases of TB endometritis cases below 35 years of age.

Clinicopathological Profile of Patients with Uterine Malignancy

There were 4 cases of endometrial carcinoma which were studied. Out of these 4 cases, 2 (50%) presented with polymenorrhoea and 2 (50%) with menorrhagia. Three of these

cases had associated complaint of excessive discharge per vaginum and 3 had not attended their menopause. The Classical Triad of 'Corpus Cancer Syndrome' i.e. *Diabetes, Hypertension and Obesity*' was seen in 2 (50%) cases.

Two (50%) cases had a large for age uterus and adenexal involvement (right adenexal mass) however, could be demonstrated in only 1 (25%) case. Two out of these 4 cases were clinically diagnosed as Fibroid uterus and two as DUB. USG was done in all 4 cases. It diagnosed 2 cases as Fibroid uterus (including one with thickened endometrium associated with right solid ovarian tumor), and rest 2 cases as DUB. All these cases could be diagnosed as endometrial carcinoma on microbiopsy. Thus, it is seen that endometrial aspiration cytology and microbiopsy should be performed in all cases of suspected malignancy.

CONCLUSION

All cases of AUB in the peri and post menopausal age group should be thoroughly analyzed including complete history, detailed clinical examination followed by appropriate radiological and pathological examination, especially in suspicious cases for early detection of premalignant and malignant lesions of the body of uterus, leading to early diagnosis and prompt treatment at appropriate time.

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